PCT10

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/009,852

DATE: 01/14/2002 TIME: 07:37:21

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Output Set: N:\CRF3\01142002\J009852.raw

ENTERED

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4 < 110 > APPLICANT: Nicholas J. Papadopoulos et al.
      6 <120> TITLE OF INVENTION: MODIFIED CHIMERIC POLYPEPTIDES WITH IMPROVED
              PHARMACOKINETIC PROPERTIES AND METHODS OF MAKING
              AND USING THEREOF
     10 <130> FILE REFERENCE: REG 710-A-US
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/009,852
C--> 13 <141> CURRENT FILING DATE: 2001-12-06
     15 <150> PRIOR APPLICATION NUMBER: PCT/US00/14142
     16 <151> PRIOR FILING DATE: 2000-05-23
     18 <150> PRIOR APPLICATION NUMBER: 60/138,133
     19 <151> PRIOR FILING DATE: 1999-06-08
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        tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta aaa gat cct
                                                                                96
        Cys Leu Leu Leu Thr Gly Ser Ser Gly Ser Lys Leu Lys Asp Pro
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    41
                                         25
        gaa ctg agt tta aaa ggc acc cag cac atc atg caa gca ggc cag aca
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        Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
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                 35
                                     40
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       ctg cat ctc caa tgc agg ggg gaa gca gcc cat aaa tgg tct ttg cct
                                                                              192
       Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
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       gaa atg gtg agt aag gaa agc gaa agg ctg agc ata act aaa tct gcc
   51
                                                                              240
       Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
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   53
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       tgt gga aga aat ggc aaa caa ttc tgc agt act tta acc ttg aac aca
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                                                                              288
       Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
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                                             90
   59
       get caa gea aac cae act gge tte tae age tge aaa tat eta get gta
                                                                              336
       Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
   60
                   100
                                        105
       cct act tca aag aag gaa aca gaa tct gca atc tat ata ttt att
   63
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       Pro Thr Ser Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
   64
   65
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                                   120
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       agt gat aca ggt aga cct ttc gta gag atg tac agt gaa atc ccc gaa
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7.3	147					150					155					160	
75	acg	tca	cct	aac	atc	act	gtt	act	tta	aaa	aaσ	+++	сса	ctt	gac	act	528
76	Thr	Ser	Pro	Asn	Ile	Thr	Val	Thr	Leu	Lys	Lys	Phe	Pro	Leu	Asp	Thr	320
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83	atc	ata	tca	aat	gca	acg	tac	aaa	gaa	ata	ggg	ctt	ctg	acc	tat	gaa	624
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88	Ala	TIII	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr	Leu	Thr	His	Arg	
89		210					215					220					
91 92	Caa	acc	aat	aca	atc	ata	gat	gtc	caa	ata	agc	aca	сса	cgc	сса	gtc	720
93	GIII	Inr	Asn	Thr	Ile	He	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val	
95 95	223					230					235					240	
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97	гуѕ	rea	reu	Arg	Gly	His	Thr	Leu	Val	Leu	Asn	Cys	Thr	Ala	Thr	Thr	
99	CCC	tta	220	200	245	4 4				250					255		
100	Dro	LLY	aac . Acn	acy The	aga	gtt	caa	atg	acc	tgg	agt	tac	cct	gat	gaa	aaa	816
101	110	, rea	I ASII	260	Arg	vaı	GIN	Met	Thr	Trp	Ser	Tyr	Pro			Lys	
103	aat	aad	ада			at a	200		265	_ 4. 4				270)		
104	Asn	Lvs	Ara	Ala	Ser	Val	Ara	Cya Ara	cya Ama	att	gac	caa	agc	aat	tcc	cat	864
105		272	275	2110	261	val	Aly	280	Arg	тте	Asp	GIn			Ser	His	
107	qcc	aac			tac	agt	att		act	a + +	<i>a</i>		285			aaa	
108	Āla	Asn	Ile	Phe	Tvr	Ser	Val	Len	Thr	Tlo	yac	daa	atg	cag	aac	aaa Lys	912
109		290			- 1 -	001	295	ьсu	1111	116	ASP	300	мес	GIN	Asn	Lys	
111	gac	aaa	gga	ctt	tat	act		cat	ata	agg	ant	200	000	+ 00	++-		0.60
112	Asp	Lys	Gly	Leu	Tyr	Thr	Cvs	Ara	Val	Ara	Ser	Glv	Dro	Con	Dho	aaa	960
113	305				•	310		9		9	315	Gry	FIU	Set	PHe		
115	tct	gtt	aac	acc	tca	gtg	cat	ata	tat	gat.	aaa	gca	aac	cca	aac	320	1000
116	Ser	Val	Asn	Thr	Ser	Val	His	Ile	Tyr	Asp	Lvs	Ala	Glv	Pro	99C	Clu	1008
117					323					330					335		
119	CCC	aaa	tct	tgt	gac	aaa	act	cac	aca	tgc	сса	cca	tac	cca	σca.	cct	1056
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121				340					345					350			
123	gaa	ctc	ctg	ggg	gga	ccg	tca	gtc	ttc	ctc	ttc	ccc	сса	222	ccc	aad	1104
124	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lvs	Pro	Lvs	1104
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128	Asp	1111	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Va Î	Val	
129		3/0					3/5					380					
131	gac	gtg	agc	cac	gaa	gac	cct	gag	gtc	aag	ttc	aac	tgg	tac	gtg	gac	1200
132 133	Asp 385	val	ser	Hls	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tvr	Val	Asp	
TOO						390							F	- 1 -		r	



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137	7	Val	. 016	ı val	405	ASI	1 Ala	т Гу:	s In	r Ly 41	rs Pr	0 A.	rg G.	Lu G.	lu		ı Tyr	
139		ago	acg	tac	cgt	gto	gto	ago	e qt	c ct	.c ac	ic ai	tc c1	-a -c	a C	415	1 020	1206
140	ASII	Ser	Thr	Tyr	Arg	[Va]	Val	. Sei	. Va	l Le	u Th	ır Va	al Le	eu Hi	is	Glr	Asp	1296
141	L			420					42	5				4	R O		•	
143 144	, , ,	ctg	aat	ggc	aag	gaç	, tac	aac	j tg	c aa	g gt	c to	cc aa	ic aa	aa	gcc	ctc	1344
145	: ith	reu	435	GIY	Lys	Glu	ı Tyr	Lys	з Су:	s Ly	s Va	1 Se			S	Ala	. Leu	
147		qcc			gag	aaa	acc	440					4.4	5				
148		Ala	Pro	Ile	Glu	Lvs	Thr	Tle	Sei	Jada r Iv	ago e 101	Caa	ia gg	g ca	ıg	CCC	cga Arg	1392
149		400					455					4.6						
151	gaa	cca	cag	gtg	tac	acc	ctg	CCC	cca	a to	c cq	or ora	t ora	a ct	a .	acc	aag	1440
152	Giu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Se:	r Ar	g As	p Ğl	u Le	·u	Thr	Lys	1110
153 155	405					4/0					47	5					190	
156		Cay	y LC Val	agc	ctg	acc	tgc	ctg	gto	aaa	a gg	c tt	c ta	t cc	C	agc	gac	1488
157		0111	vai	261	485	1111	Cys	Leu	Va I	. Lys 490	5 G1;	y Ph	е Ту	r Pr			Asp	
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161				300					505					5.1	\cap			
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164 165	Thr	Thr	PIO	Pro	Val	Leu	Åsp	Ser	Asp	Gly	sei	. Ph	e Ph	e Le	u :	Гуr	Ser	1301
167			\mathcal{I}					520					52	5				
168	Lvs	Len	Thr	Val	yac Aen	aag	agc	agg	tgg	cag	cac	ı gg	g aad	e gti	c t	tc	tca	1632
169	Lys	530	1111	, u 1	пэр	гуз	535	AIG	тгр	GIN	GIr	1 GI	y Ası	ı Va	l F	Phe	Ser	
171	tgc Cvs	tcc	gtg	atg	cat	gag	qct	cta	cac	aac	cac	540 tao	3 200		• ~		200	1600
172	Cys	Ser	Val	Met	His	Ğlu	Åla	Leu	His	Asn	His	Tvi	r Thi	r Cay	y a n I	.vs	ayc Ser	1680
173	243					220					555	4 -		011		1,5	560	
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188	_)					10					1	5		
189	Cys I	.cu 1	20 u 1	20 .	1111 (зту.	ser ;	ser	ser 25	GIY	Ser	Lys	Leu		Α.	sp 1	Pro	
190	Glu I	eu S			Lys (Glv '	Thr (iln	25 His	Tle	Met	Gln	λΙο	30	C	1	T) }	
191		3))				4	10					15					
192	Leu H	is I	eu 🤄	Sln (ys A	Arg (Gly (Glu .	Ala	Ala	His	Lys	Trp	Ser	Lε	eu F	Pro	
193	J	U					25					60						
194 195	Glu M 65	et V	al S	er L	ys C	Slu S	Ser (lu A	Arg	Leu	Ser	Ile	Thr	Lys	Se	er A	Ala	
196	0.5				. /	· U					75						2.0	
	Cys G	+1 A	-y A	.511 (т У Г	ys (3 T I I F	me (_ys	ser	Ihr	Leu	Thr	Leu	Αs	sn I	Thr	



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198	Al	a Gl	n Ala	a Ası		s Thi	r Gla	. Phe	= T <i>ur</i> i			c Iv	с т	r T 0	95	a Val
199				100)		. 01		105	5	т су	s Ly	5 I).	110		a val
200	Pr	o Th	r Se	r Lys	s Ly:	s Lvs	s Gli	ı Thi			r Al	a Tla	5 T++	TIU TIU	J Db.	e Ile
201			115	5	-1	7 -	, 010	120)	1 50.	ı Aı	1 11	≘ 1y. 12:		e Phe	e 11e
202	Se.	r As	p Thi	r Glv	z Arc	ı Pro) Phe			ı Mo	t T++	r Co.	141) . т1.		o Glu
203		13	0	1		, , , ,	135	- •u.	. 010	i ne	С ТУ.			1 116	e Pro	o Giu
204	Ile	e Ile	e His	s Met	Thi	c Glu			r Cli	1 T 01	. 1/2	140	<i>J</i>		_	g Val
205	145	5			- 1111	150	. Оту	. VI č	, GIC	ı re	15:		e Pro	o Cys	s Arg	
206	Thi	r Se:	r Pro) Asr	Tle			Thr	- T O	T 11.0	IJ.) . Db.	. D		_	160 Thr
207					165	, 1111	va 1	. 1111	Leu	г _{Буз}		s PHE	Pro	Leu		
208	Lei	1 Ile	e Pro	Asn			Δra	Tle	Tlo	1/(T~~) 				175	y Phe
209				180	011	LŢJ	A. y	116	185	. 1TF	AS	ser	Arg			7 Phe
210	Ιlε	: Ile	Ser			Thr	Tur	Tvo					-	190	_	Glu
211			195	11011	1110	1111	тут	200	GIU	116	; GT	Lei			. CAs	Glu
212	Ala	Thr			Glv	Hic	Lou			The			205			
213		210)	11011	Ory	1113	215	тут	гуѕ	1111	ASI			Thr	His	Arg
214	Glr			Thr	Tlo	Tlo			Cl.	т1.	<i>a</i> .	220	_	_		
215	225		11511	1111	110	230	ASP	val	GIII	116			Pro	Arg	Pro	Val
216			Leu	Ara	Glv		Thr	Lou	1751	Ť o.u	235		æ 1	- 3	_ ,	240
217	-72	Dea	ВСС	my	245	1112	1 1111	Leu	Val	Leu	Asn	Cys	Thr	Ala		Thr
218	Pro	Len	Asn	Thr			Cln	Mot	The	250		_	_		255	
219		-200	11011	260	1119	Val	GIH	Met	265	пр	ser	Tyr	Pro		Glu	Lys
220	Asn	Lvs	Ara		Sar	Val	λνα	λκα		т1.		0.1	-	270		
221		-10	275		JCI	Val	nig	280	Arg	116	ASP	GIN		Asn	Ser	His
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225	305	-1-	0-1	Deu	+ 1 -	310	Cys	hiy	val	AIG	315	GIY	Pro	Ser	Phe	
226	Ser	Val	Asn	Thr	Ser	Val	His	ΤlΔ	Tur	λαρ	217	7. 1 ~	C1	D	a.1	320
227					325	141	1115	116	тут	330	ьуѕ	Ald	GIA	Pro		Glu
228	Pro	Lys	Ser	Cvs		Lys	Thr	Hic	Thr	220	Dro	Dwo	C	D	335	
229		1		340				1113	345	Суз	PIO	PIO	Cys		Ата	Pro
230	Glu	Leu	Leu	Glv	Glv	Pro	Ser	Va 1	Dho	Lou	Dho	Dro	Dwa	350	D	.
231			355	1	1		501	360	1 116	ьeu	FIIE	PIO	365	Lys	Pro	Lys
232	Asp	Thr	Leu	Met	Ile	Ser	Ara	Thr	Pro	Glu	V=1	Thr	202	17 - 1	17.0 1	17- 1
233		370					375	1111	110	GIU	Val	380	Cys	vaı	vai	vaı
234	Asp	Val	Ser	His	Glu	Asp		Glu	Va l	Luc	Dho	300 300	Trn	T	u. 1	3
235	385					390				цуз				1 7 1		
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237	-				405			273	1111	410	FIU	MIG	GIU	GIU		Tyr
238	Asn	Ser	Thr			Val	Va 1	Ser	Va l	Leu	Thr	Val	T OU	Hia	415	3
239				420)			DCI	425	ьец	1111	val	Leu	430	GIN	Asp
240	Trp	Leu	Asn	Glv	Lvs	Glu	Tvr	Lvs		Tue	V = 1	Cor	λαη	430	n 1 -	T .
241	_		435	1			- 1 -	440	Cys	цуз	Val	ser	445	Lys	Ата	Leu
242	Pro	Ala	Pro	Ile	Glu	Lys '			Ser	Lve	Δla	Lve	71.7 71.7	Cln	Dro	7
243		450			==	1-	455		JC1	Lys	11 I C	460	оту	GTII	LTO.	Arg
244	Glu	Pro	Gln	Val	Tyr	Thr		Pro	Pro	Ser	Δra	Zen	Clu	Low	Th∽	Tira
245	465				4	470		0			475	wah	GIU	Leu		
											4/3					480



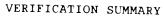
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248		e Al	la Va	al Gl	48 u Tr		11 Se	er Ac	n G1	49	90 n Dr		7		49	5 T Lys	
249	,			Dυ	i U				5.0	15				5.1	Λ		
250 251	-		91	.)				52	:0				5.2	ie Le	eu Ty	r Ser	
252 253	Ly	s Le	eu Th	ır Va	l As	p Ly	s Se	r Ar	g Tr	p Gl	n Gl	n Gl	y As	n Va	l Ph	e Ser	
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290 291	Cys	GLY	Arg	Asn	GIY	Lys	Gln	Phe	Cys	Ser	Thr	Leu	Thr	Leu	Asn	Thr	200
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294	Ala	Gln	Ala	Asn	UaC Hie	act	ggc	Dho	tac	agc	tgc	aaa	tat	cta	gct	gta	336
295				100	1113	1111	сту	Pne	105	ser	Cys	Lys	Tyr		Ala	Val	
297	cct	act	tca	aag	aag	aaq	gaa	aca	gaa	tat	gca	atc	tat	110	ttt	2++	204
298	Pro	Thr	Ser	Lys	Lys	Lys	Ğlu	Thr	Glu	Ser	Ala	Ile	Tvr	Tle	Phe	alt Tle	384
299			117					120					125				
301 302	agt	gat	aca	ggt	aga	cct	ttc	gta	gag	atg	tac	agt	gaa	atc	CCC	gaa	432
302	set.	130	ınr	GIY	Arg	Pro	Phe	Val	Glu	Met	Tyr	Ser	Glu	Ile	Pro	Glu	
305		100					135					140					
306	Ile	Ile	His	Met.	Thr	Glu	yya Gl∵	ayy Ara	gag	CEC	gtc	att	CCC	tgc	cgg Arg	gtt	480
						J _ U	O T Y	17 L Y	GIU	ьеu	val	тте	rro	Cys	Arg	Val	



PAIENT APPLICATION: US/10/009,852

DATE: 01/14/2002 TIME: 07:37:22

Input Set : A:\REG710AUS3.txt

Output Set: N:\CRF3\01142002\J009852.raw

L:12 M:270 C: Current Application Number differs. Replaced Current Application Number

L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date